REMARKS/ARGUMENTS

With this amendment, claims 21-8, 16, 28, and 29 are pending. Claims are cancelled without prejudice to subsequent revival. For convenience, the Examiner's rejections are addressed in the order presented in a March 2, 2004 Office Action.

I. Status of the claims

Claims 1, 16, and 28 are amended to recite "A purified antibody that binds a frizzled 5 receptor". Support for this amendment is found throughout the specification, for example, at page 18, lines 15-17. Claims 1 and 16 now recite in the body of the claim, rather than the preamble, that the frizzled 5 antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor. Support for these amendments is found throughout the specification, for example, at page 22 lines 4-6. Claim 28 now recites in the body of the claim, rather than the preamble, that the frizzled 5 antibody is effective for immunotherapy of a malignant cell that overexpresses the frizzled 5 receptor. Support for this amendment is found throughout the specification, for example, at page 21, line 24 through page 22, line 2; at page 25, lines 1-5; and at page 26, lines 6-13. These amendments are not limiting amendments and add no new matter.

Claim 5 is amended to recite that the antibody interferes with signaling through the Frizzled 5 signaling pathway. Support for this amendment is found throughout the specification, for example at Figure 1; at page 7, lines 19 through page 8, line 2; and at page 22, lines 7-9. This amendment adds no new matter.

II. Rejections under 35 U.S.C. §112, first paragraph, written description

Claim 5 is rejected under 35 U.S.C. §112, second paragraph for allegedly failing to comply with the written description requirement. In order to expedite prosecution and at the request of the Examiner, claim 5 is amended to recite that the antibody interferes with signaling through the Frizzled 5 signaling pathway. Frizzled 5 is a member of the frizzled protein family disclosed throughout the specification, *e.g.*, at page 8, lines 3-5 and at Table I, page 9. The Wnt/Frizzled signaling pathway is described in the specification, *e.g.*, at page 7, lines 19 through

page 8, line 2. Interference with the pathway is described, *e.g.*, at page 22, lines 3-9. In view of this amendment, Applicants respectfully request withdrawal of the rejection.

III. Rejections under 35 U.S.C. §103(a)

Claims 1-8, 16 and 28-29 are rejected under 35 U.S.C. §103(a) as allegedly obvious over any one of Tanaka *et al.*, He, *et al.*, or Wang *et al.* in view of Campbell. The Office Action appears to assert that the claims are directed to all antibodies that recognize the Frizzled 5 protein.

To the extent the rejection applies to the amended claims, Applicants respectfully traverse. The Office Action has not established a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference must teach or suggest all the claims limitations. MPEP§2143. See also *In re Rouffet,* 47 USPQ2d 1453. The court in *Rouffet* stated that "even when the level of skill in the art is high, the Board must identify specifically the principle, known to one of ordinary skill, that suggests the claimed combination." *Rouffet* at 1459. The court has also stated that actual evidence of a suggestion, or teaching, or motivation to combine is required and the showing of a suggestion, or teaching, or motivation to combine must be "clear and particular." *In re Dembiczak*, 50 USPQ2d 1614, 1617 (1999).

According to the Office Action, the claims are drawn to an antibody that binds to SEQ ID NO:68 and language of the preamble does not limit the claims. In order to expedite prosecution, independent claims 1, 16, and 28 are amended to move a phrase from the preamble to the body of the claim. Thus, the body of claims 1 and 16 now recite that the antibody inhibits growth of a malignant cell that expresses the frizzled 5 receptor and the body of claim 28 recites that the antibody is effective for immunotherapy of a malignant cell that overexpresses the frizzled 5 receptor.

The claims are directed to antibodies that bind to the amino terminal extracellular domain of the frizzled 5 receptor, and that inhibit growth of a malignant cell that expresses the frizzled 5 protein. The claimed invention is based, at least in part, on the recognition that frizzled proteins, including frizzled 5, are overexpressed in some cancers, and thus, can be used as tumor specific antigens that can be used to generate immunotherapy agents. The claimed antibodies are immunotherapy agents used to inhibit growth of or kill cancer cells. None of the cited references provide evidence that the frizzled 5 protein is overexpressed in malignant cells or that antibodies directed against frizzled 5 are useful to kill cancer cells that express frizzled 5. As such, the claimed antibodies are a patentably distinct species of the broad genus of Frizzled 5 antibodies, referred to by the Office Action. Without recognition of the role of frizzled proteins in cancer, antibodies against frizzled proteins would be raised only to function as research tools, not as growth-inhibiting, immunotherapeutic agents as required by the claims. In addition, none of the cited references disclose the specifically claimed amino terminal extracellular domain of frizzled 5 or antibodies against that domain.

Tanaka *et al.* disclose the cloning of the frizzled 7 gene and report that frizzled 7 is overexpressed in esophageal cancer. Tanaka *et al.* disclose a portion of frizzled 5 amino acid sequence (not the same as SEQ ID NO:68) and further show that expression of frizzled 5 is not correlated with esophageal cancer (see, *e.g.*, Figure 1). Thus, Tanaka *et al.* fail to disclose the claimed amino terminal extracellular frizzled 5 sequence and, in fact teach away from a role for frizzled 5 in cancer. Because of that failure, the disclosure of Tanaka *et al.* also fail to provide evidence of a motivation to identify antibodies directed against frizzled 5 that inhibit proliferation of cancer cells.

He *et al.* disclose a role for frizzled 5 and wnt 5A in development, but do not disclose any role for frizzled 5 in cancer. In addition, He *et al.* cite Wang *et al.* for the frizzled 5 sequence and do not provide any other frizzled 5 sequence or subsequence. Thus, He *et al.* do not provide the claimed frizzled 5 sequence or evidence of a motivation to use that sequence to produce antibodies against frizzled 5 that inhibit proliferation of cancer cells.

Wang *et al.* disclose the full length sequence of frizzled 5 but do not disclose the amino terminal extracellular domain of frizzled 5 or its use to make the claimed antibodies.

Therefore, Wang *et al.* do not teach the amino terminal extracellular domain of frizzled 5 as is claimed. Wang *et al.* do not disclose a role for frizzled 5 in cancer and thus do not provide evidence of a motivation to identify antibodies against the amino terminal extracellular domain of frizzled 5 that inhibit proliferation of cancer cells.

Campbell discloses only general methods to make antibodies. Campbell does not disclose or suggest using the amino terminal extracellular domain of frizzled 5 to produce antibodies and does not provide a particular showing of the use of frizzled 5 antibodies as immunotherapeutic agents. Thus, Campbell does not provide evidence of a motivation to combine the cited references to arrive at the claimed invention.

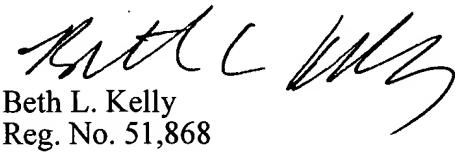
In summary, alone or in combination, the cited references do not disclose all the elements of the claimed invention and do not provide evidence of a motivation for their combination to arrive at the claimed invention. In view of the above amendments and remarks, withdrawal of the rejection is respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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